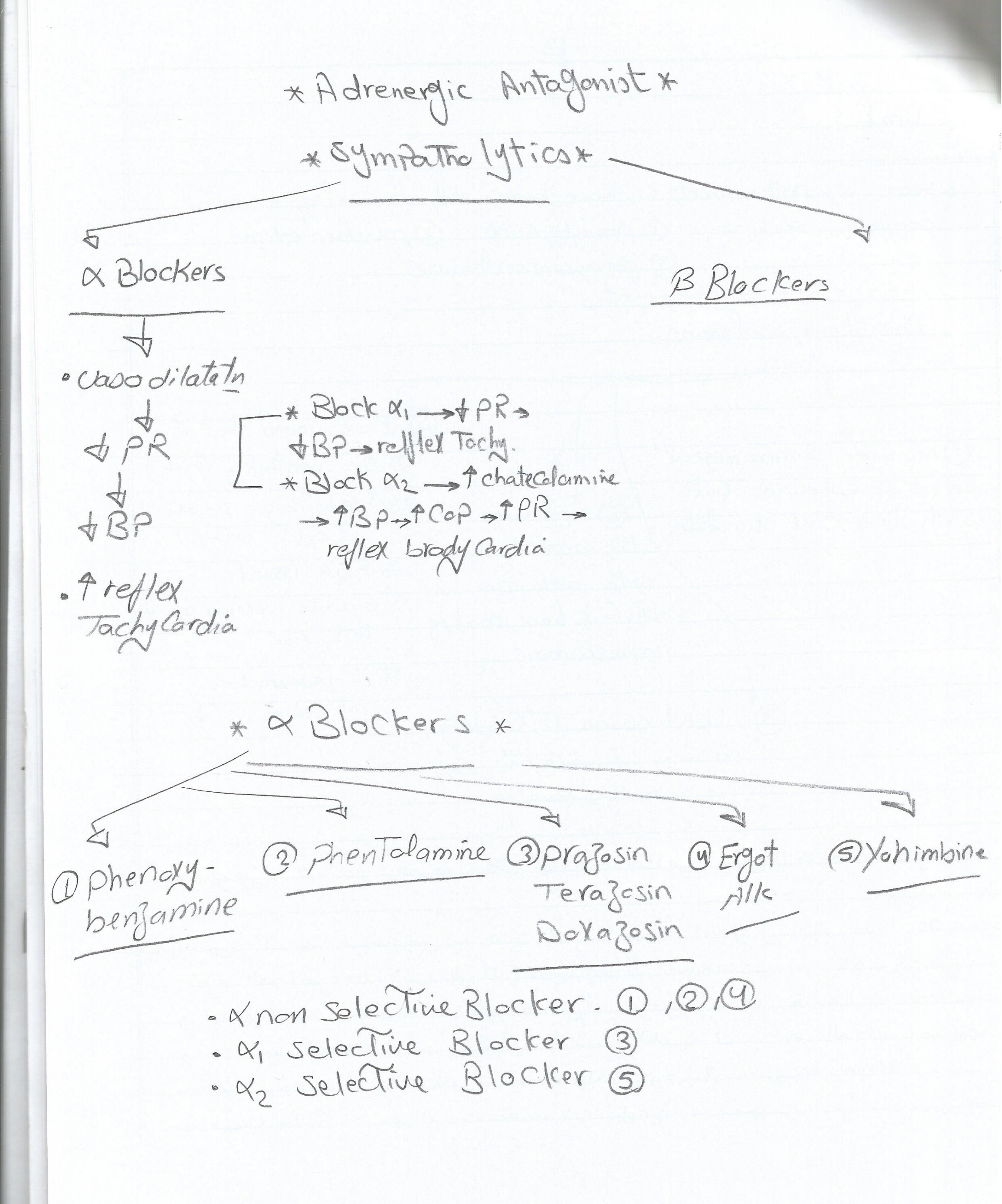


* Adrenergic Antagonist *

* Sympatholytics *

α Blockers

- vasodilatation
  ↓
  ↓ PR
  ↓
  ↓ BP
- ↑ reflex Tachycardia

* Block α_1 → ↓ PR → ↓ BP → refflex Tachy.
* Block α_2 → ↑ chatecolamine → ↑ BP → ↑ COP → ↑ PR → reflex bradycardia

β Blockers

* α Blockers *

① phenoxy-benzamine

② Phentolamine

③ prazosin, Terazosin, Doxazosin

④ Ergot Alk

⑤ Yohimbine

- α non selective Blocker - ①, ②, ④
- α_1 selective Blocker ③
- α_2 selective Blocker ⑤

خد نفس عميق
أوي ده علشان المشوار
كبير ده بس حلو
ولذيذ صدقني .
يلا بينا معالي .

Adrenergic antagonists

- α_Blockers
- B_Blockers

أنا بأعمل كده علشان
تبقى عارف إحنا ماشيين
إزاي وماتوهش مني .
ركز بقا و صحصح صاحبي .
للكوباية شاي كده ويلا معايا .

α_Adrenergic Blockers

1. phenoxybenzamine
2. phentolamine
3. Praznsin, terazosin, doxazosin
4. Ergot Alkaloids
5. yohimbine

*→ U have to Know that those agents mainly affect Blood pressure

*→ Blocking of α receptors → induce vasodilatation → ↓PR → ↓Blood pressure

*→ this induces reflex tachycardia from lowered BP.

وكده شرحنا قبل كده يعني إيه reflex tachycardia و reflex bradycardia.

(1) Phenoxybenzamine

- (a) Concept of action.
- (b) actions.
- (c) Therapeutic uses.
- (d) adverse effects.

I Pheoxy Benzamine α Blocker

A MoA

- Drugs Related to Nitrogen mustards
- α nonselective B.
  - α_1 → Postsynaptic
  - α_2 → pre "
- Non Competitive and To overcome This Blocking is ↓ body synthesis new R_s
- Prodrug —body / Biotransformatn→ Active form

B Actn

- α_1 B → Vasodilatatn → ↓PR → ↓BP → reflex Tachycardia
- α_2 B → ↑catecholamines → ↑ COP
- Epinephrine reversed why?
- → phenoxy Benzamine Block α effect of epinephrine → Vasodilatn → ↓PR → ↓BP
- → phenoxy Benzamine not affect β_2 effect of epinephrine → Vasodilatatn → ↓PR → ↓BP
- Nor epinephrine not reversed by only its Actn is decreased. as Nor epinephrine has ↓ effect on B R_s
- Isoproterenol not affected by phenoxy Benzamine as it pure B Agonist

C Therapeutic uses

1. in surgecal removal of pheochromocytoma (tumor of Adrenal medulla ???)
2. in Raynaud's Disease الاطراف بتنمل

D Adverse effect

1. Postural hypotension (orthostatic - ???)
2. Nausea. Vomiting nasal stiffness
3. ↓ male ejaculatn (↓vasoconstrictn)
4. ↑ reflex Tachy Cardia → C.I in patient c̄ Cronory Perfusion ???

ⓐ Concept of action :

* it's a drug related to nitrogen mustards.
* it's a non-selective blocker → bind covalently to (α_1) post synaptic , (α_2) presynaptic receptors.
* this block is irreversible , non competitive

يعني ملوش حل ← مش هاقدر أشيله بإني أزود الـ agonist ولا إني أكسر الـ bond اللي بينه وبين الـ receptor.

طيب إيه الحل يعني؟

* the only mechanism to overcome this block is that the body synthesize new receptors
  → this will take a day or more. (24 hrs)
* it's action is slow (delayed) → as it's a prodrug → requires Biotransformatn, to change to its active form.

يعني بياخد وقت علشان يشتغل و بياخد وقت علشان يقف.

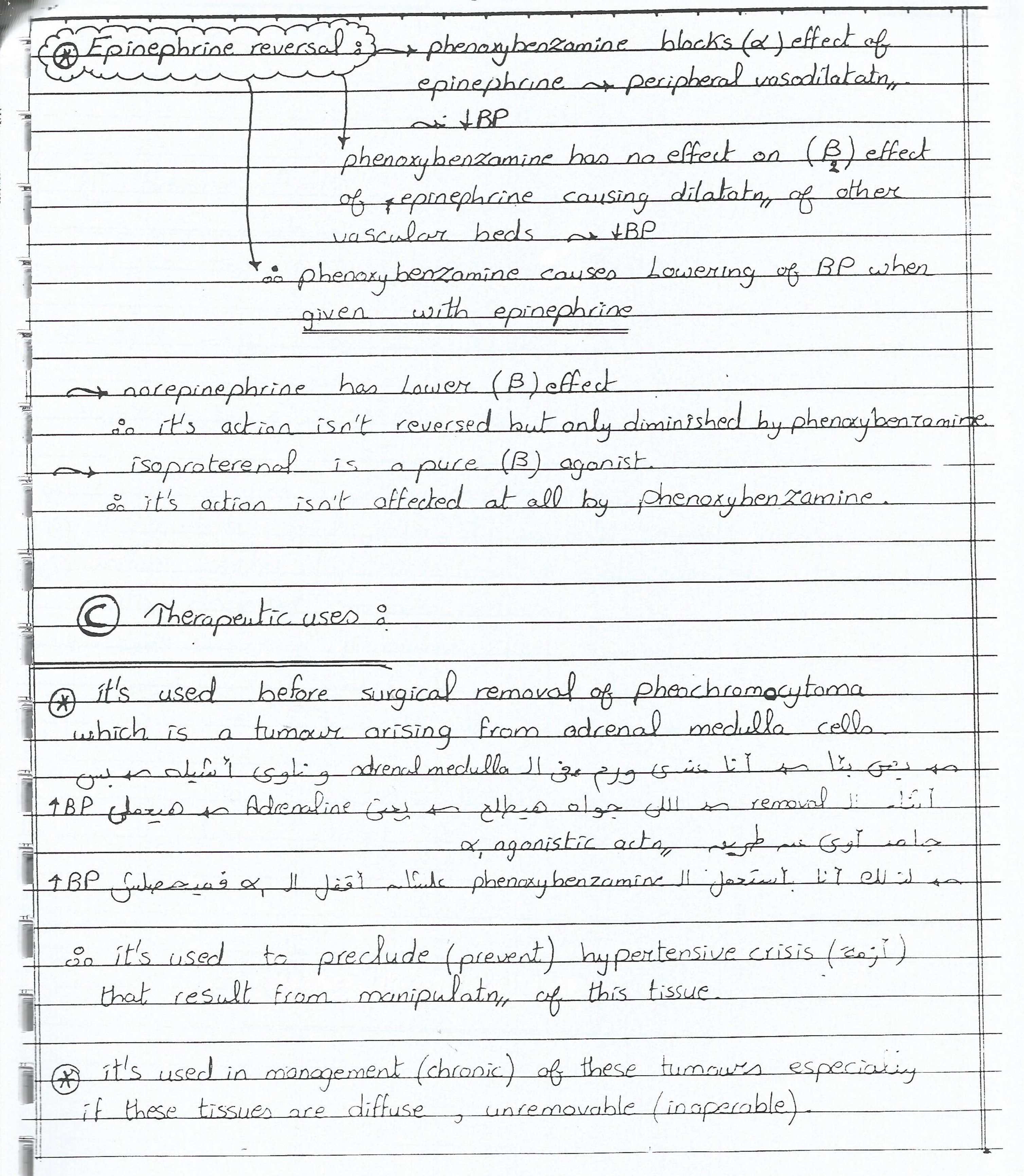
ⓑ Actions :

* Blocks (α_1) receptors → Vasodil. → ↓PR → ↓BP → reflex tachycard.
* Blocks (α_2) presynap on heart → ↑ catecholamine release on heart causing ↑ in Cardiac output.

آكيد حد هيسأل ويقول ← هو إنت مش قلت إن القلب ماعليهوش غير (β_1)؟ ← هاجاوب ← يا حبيبي أنا بقول هنا ← يعني على الـ nerve اللي جاي للقلب ← مش الـ receptor اللي على القلب نفسه.

→ So → reflex tachycardia + ↑ COP → ∴ ↑BP

∴ the effect of phenoxybenzamine in ↓BP is small ∴ its use is discontinued



⊛ **Epinephrine reversal :** → phenoxybenzamine blocks (α) effect of epinephrine → peripheral vasodilatatn → ↓BP

→ phenoxybenzamine has no effect on (β_2) effect of epinephrine causing dilatatn of other vascular beds → ↓BP

∴ phenoxybenzamine causes lowering of BP when given with epinephrine

→ norepinephrine has lower (β) effect
∴ it's action isn't reversed but only diminished by phenoxybenzamine.

→ isoproterenol is a pure (β) agonist.
∴ it's action isn't affected at all by phenoxybenzamine.

Ⓒ Therapeutic uses :

⊛ it's used before surgical removal of pheochromocytoma which is a tumour arising from adrenal medulla cells

← يعني بنا ← أنا عندي ورم في الـ adrenal medulla وناوي أشيله ← بس أثناء الـ removal ← اللي جواه هيطلع ← يدي Adrenaline ← هيعملي ↑BP جامد أوي عن طريق α_1 agonistic actn

← فـ لذلك أنا باستعمل الـ phenoxybenzamine علشان أقفل الـ α_1 فـ ميعملش ↑BP

∴ it's used to preclude (prevent) hypertensive crisis (أزمة) that result from manipulatn of this tissue.

⊛ it's used in management (chronic) of these tumours especially if these tissues are diffuse, unremovable (inoperable).

⊛ Sometimes → its used in Raynaud's disease

يعني الواحد تبقى أطرافه ساقعة أوي ← أديله phenoxybenzamine يعمل peripheral vasodil. ← الدم يوصل للأطراف ← تدفى.

Ⓓ Adverse effects :

⊛ it can cause postural hypotension (orthostatic hypotension)

يعني إيه؟

← إنت لما بتيجي تقف فجأة ← المفروض إن ال α بتشتغل ← ↑PR ← ↑BP علشان يوصل الدم للمخ

← أنا لو واخد phenoxybenzamine ← ال α مش هتشتغل ← هيحصل hypotension بنسميه Postural hypoten. ← فبتحس بدوخة جامدة

⊛ it causes nausea, vomiting, nasal stiffness

⊛ it inhibits male eJaculatn. → as it prevents vasoconstrictn.

⊛ induce reflex tachycardia → ∴ contraindicated with patients with decreased coronary perfusion

يعني لو واحد عنده مشكلة في ال coronary artery اللي بيغذي عضلة القلب نفسها ← المفروض إن أهدي القلب علشان هو مش واخد غذاء ولا O_2 كويس ← لذلك لو سرعته هيحصل مشاكل في عضلة القلب نفسها

← كده إحنا خلصنا ال Phenoxybenzamine ← هو مخلش طويل بس النيد وممكن تلخصه إنت مع نفسك لو فهمت ال concept بتاعه كويس.

← تعالوا نشوف ال

② Phentolamine → ⓐ Concept of actions
→ ⓑ actn., uses, adv. eff.

Phenoxy Benzamine أو (2) Phentolamine α Blocker

A MoA

- non selective α Blocker
- الغير Competetive

B Actn

- α_1 B → Vasodilatn → ↓ PR → ↓BP → reflex Tachy cardia
- α_2 B → ↑ Catecholamines → ↑ COP
- Epinephrine reversal ↓ BP
- Nor Epinephrine ↓ its Actn
- not affect Isoproterenol

C Therapeutical uses

① only in diagnosis of Pheochromocytoma but phenoxy Benzamine used in ttt and surgery why ??? as its effect for short Time (competitive)

D Adverse effect

① Postural hypotension
② Nausea. Vomiting nasal stiffness.
③ Angina + Arrythmia due To ↑ reflex Tachycardia in Patient ē coronary Perfusion

(a) Concept of action :

زي الـ phenoxybenz بالضبط من القوي الوحيد أنه competitive , reversible

وده مهم جداً في التفرقة بين الـ action بتاعه وبتاعها.

(*) it's non selective blocker → blocks (α_1) postsynaptic , (α_2) presynaptic

(*) this block is reversible , competitive

→ so its actn lasts for 4 hrs only.

(b) actions :

بالضبط زي الـ phenoxybenzamine

(*) Blocks (α_1) → Vasodil. → ↓PR → ↓BP → reflex tachycardia mediated by baroceptors (baroreceptors).

(*) Blocks (α_2) presynaptic on heart → ↑ catecholamine release → ↑ COP

(*) epinephrine reversal → causes ↓BP when taken with Phentolamine.

(c) uses :

بتاعة الـ phenoxybenzamine

(*) used in diagnosis of pheochromocytoma.

↓

only diagnosis → علشان الـ effect بتاعه قصير

الـ phenoxybenzamine بنستخدم في الـ treatment و في الـ surgery

علشان الـ effect بتاعه طويل الزمن

(d) adverse effects :

زي الـ phenoxybenzamine بالضبط

(*) Postural hypotension (orthostatic hypotension)

(*) arrhythmiasis , anginal pain due to tachycardia in case of patients with decreased coronary perfusion.

مش بتفرق الـ phentolamine سهل أوي بعد phenoxybenzamine

3) Perazosin - Terazosin - Doxazosin α_1 Blocker

A) MoA

- Selective α_1 Blocker
- Competetive
- metabolized To inActive sub excreted in urine except Doxazosin → feaces.
- Doxazosin have longest Actn

B) Actn

- α_1 Blocker → vaso. dilatatn → ↓PR → ↓BP → reflex Tachy cardia

N.B it is selective α_1B not α_2 ∴ not ↑ CoP

∴ used Ⅲ of hypertenion ≠ phentolamine, phenyl Benzamine

C) Therapeutical uses

1) Ⅲ of hypertension

N.B ⊥ First Dose effect → strong Hypotesion → fainting so first dose must be decreased to $\frac{1}{3}$ - $\frac{1}{4}$ of N-value. or Taken at bed Time.

2) instead of surgery used Ⅲ of prostatic hypertrophy - ???

→ α_1 Blocker → relaxatn of smooth muscles - sphincter of Bladder → urine flow.

D) Adverse effect

1- drowsiness - headach nasal congestn

2- postural hypotension

3- must be ↓ + β Blocker - Diuretics

N.B not affect male sexual functn like phenoxy Benzamine + phentolamine

③ Perazosin, Terazosin & Doxazosin

→ ⓐ Concept of actn
→ ⓑ Actions
→ ⓒ Therap. uses
→ ⓓ adverse effects.

ⓐ Concept of action :

- ⊛ They are <u>Selective, Competitive</u> (α_1) blocker.
- ⊛ Metabolism lead to inactive products → excreted in urine. except doxazosin (in feaces).
- ⊛ Doxazosin is Longest in actn.

ⓑ Actions :

- ⊛ They Block (α_1) → Vasodil. → ↓PR → ↓BP → <u>may</u> induce reflex tachycardia
- ⊛ But they don't affect (α_2) presynaptic
  ∴ no ↑ in catecholamine release at heart
  So no ↑ in COP
- ⊛ So, these drugs are effective in treatment of hypotension
  عكس phenoxybenzamine, phentolamine اللي ← لأنها مش ~~[illegible]~~ بيعملوا.
- ⊛ they cause minimal changes in COP, renal Blood flow, glomerular filteratn rate.

ⓒ Therapeutic uses :

- ⊛ <u>treatment of hypertension</u> with <u>no tolerance</u> to their actn
- ⊛ "First dose effect" → the first dose of these drugs produce

a very strong (exaggerated) hypotensive effect → that causes syncope (fainting) إغماء

∴ the first dose must be ~~to~~ decreased to $\frac{1}{3}$ or $\frac{1}{4}$ of normal dose or Given at bed time.

(*) can be used instead of surgery in patients with benign prostatic hypertrophy

(because) α_1 block → ↓ smooth muscle contractn → relaxatn of sphincter of bladder → improves urine flow

prostate gland

urinary bladder sphincter

أنا لو عندي prostate hypertroph ← هتقفل قوية الـ sphincter فتقفل الـ urine flow

← أنا لما باخد α_1 blocker ← هيعمل relaxatn الـ sphincter فتفتح قوية

فترجع الـ urine flow ← يبقى Normal ← يعني ما شيل الـ prostate خالص.

(D) Adverse effects :

(*) dizziness, drowziness, headache, nasal congestn, lack of energy.

(*) Postural hypotension (orthostatic hypotension) → in a lower degree than phenoxybenzamine, phentolamine زيهم بس أقل

(*) its dose must be ↓ if used in combinatn with a diuretic or with β Blocker.

(*) Male sexual functn isn't affected like in phenoxybenzamine, phentolamine

4) Ergot Alkaloids α Blocker

- first sympatholytics is discovered
- it is considered Partial Agonist ?? or Antagonist α R. / D R / serotonin R

5) Yohimbine α_2 Blocker

→ like reserpine in structure
→ α_2 Competitive Blocker
→ CNS → ↑ motor Activity → Tremors
→ ↑ Catecholamines Release → ↑ COP → ↑ HR
↑ BP (SBP)
→ used in Tt of male sexual dysfunctn
As cause vasoconstrictn

N.B clonidin is α_2 Agonist
& Yohimine is α_2 Antagonist

④ Ergot Alkaloids

- ⊛ The first adrenergic receptors antagonist to be discovered.
- ⊛ They act as partial agonist or antagonist at (α) receptors, dopamine receptors, serotonin receptors

إيه يا عم ال partial agonist ده؟ ـه إحنا مش بنتكلم دلوقتي عن ال antagonists
إيه اللي جاب سيرة ال agonists دلوقتي؟

→ Partial agonist means produces very little effect, blocks the receptor for in face of more potent drugs

يعني بيعطي effect قليل جداً، ولو هناك أي drug له effect تاني عايز يمسك في ال receptor ـه مش هيعرف لأن ال partial agonist موجود

⑤ Yohimbine

- ⊛ found in Bark of tree yohimbe, Rauwolfia roots
- ⊛ its structure is similar to that of reserpine.
- ⊛ it's an (α_2) competitive antagonist.

- ⊛ enters CNS → enhances motor centre activity → produces tremors
- ⊛ it ↑ HR (heart rate), ↑ COP → ↑ BP. (especially systolic BP)
- ⊛ Used in treatment of male sexual disfunction, as it ↑ Sympathetic activity by (α_2) presynoptic inhibition.

- ⊛ those effects are opposite to those of clonidine (α_2 agonist)

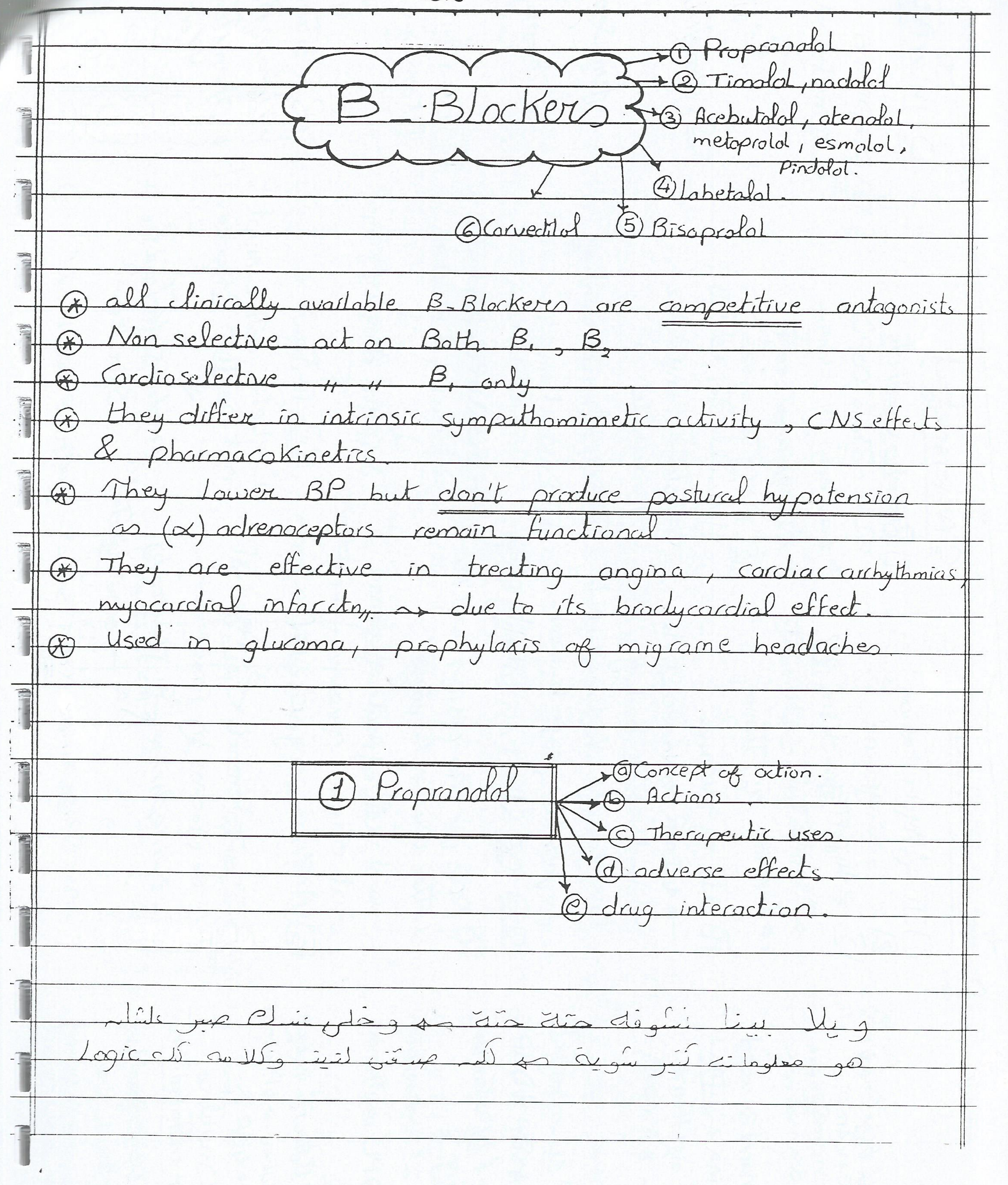
كده إحنا خلصنا ال α-blockers ـه تعالوا نشوف ال β Blockers

* β Blocker *

- Non Selective Competitive Blocker
- selective only β_1 (cardioselective)
- ↓BP but not produce hypotension (Postural) like α Blocker
- III Angina - arrythema - myocardial infarctn
  → bradycardia effect
- III of glucoma.

* β Blocker *

1. propranolol
2. Timolol
   nadolol
3. Acebutolol
   aTenolol
   metaprolol
   esmolol
   pindolol
4. labetalol
5. Bisoprolol
6. Carvedilol



B_Blockers

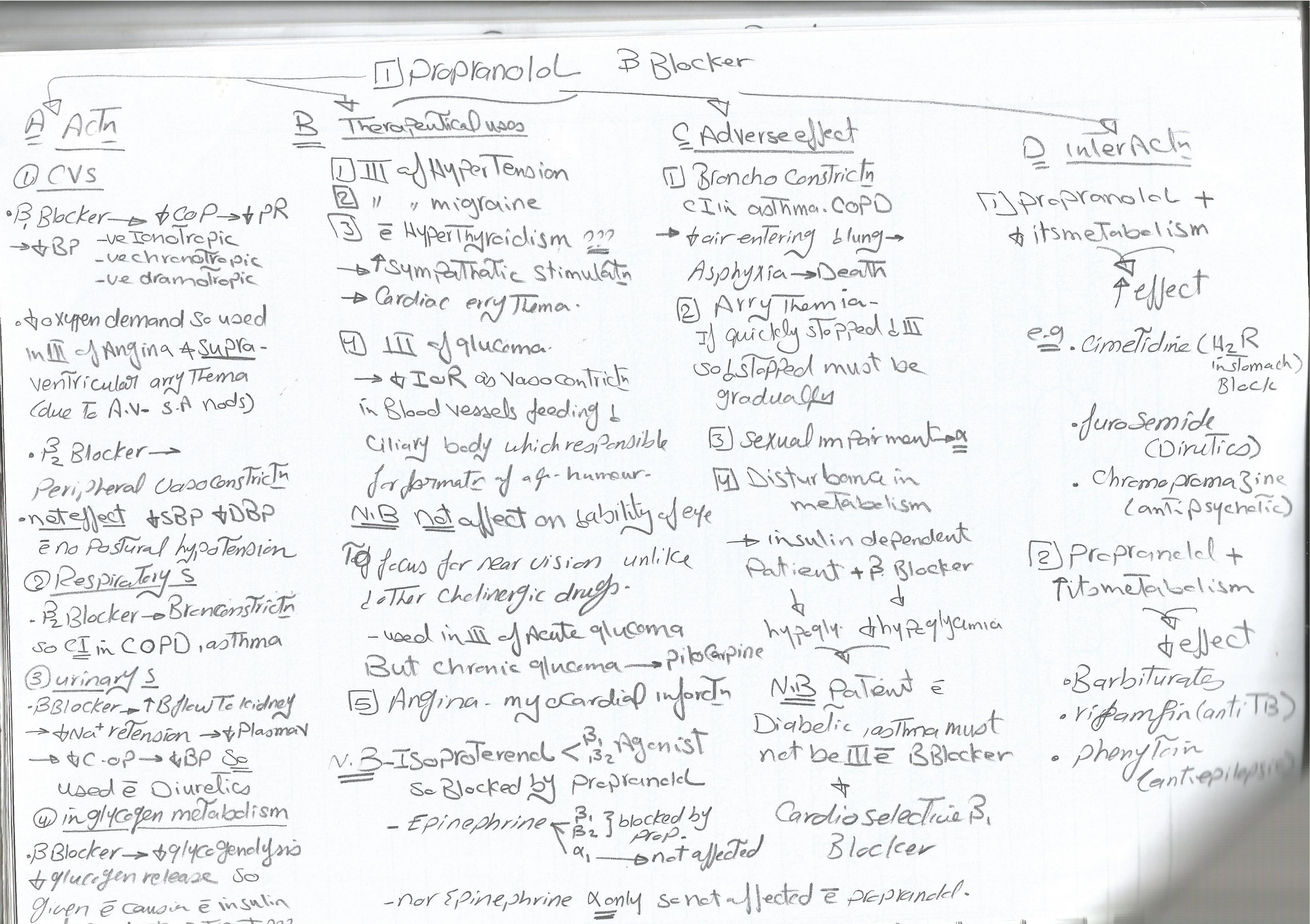
1. Propranolol
2. Timolol, nadolol
3. Acebutolol, atenolol, metoprolol, esmolol, Pindolol.
4. Labetalol.
5. Bisoprolol
6. Carvedilol

- all clinically available β-Blockers are <u>competitive</u> antagonists
- Non selective act on Both β_1, β_2
- Cardioselective " " β_1 only
- they differ in intrinsic sympathomimetic activity, CNS effects & pharmacokinetics.
- They lower BP but <u>don't produce postural hypotension</u> as (α) adrenoceptors remain functional.
- They are effective in treating angina, cardiac arrhythmias, myocardial infarctn. → due to its bradycardial effect.
- Used in glucoma, prophylaxis of migraine headaches

① Propranolol

- ⓐ Concept of action.
- ⓑ Actions
- ⓒ Therapeutic uses.
- ⓓ adverse effects.
- ⓔ drug interaction.

ويلا بينا نشوفه حتة حتة ... وخلي نفسك صبر علشان
هو معلومات كتير شوية ... لكن صدقني لذيذ وكلامه كله Logic



[1] Propranolol β Blocker

A. Actn

① CVS

- β_1 Blocker → ↓ CoP → ↓ PR → ↓ BP
  - -ve Ionotropic
  - -ve chronotropic
  - -ve dramotropic
- ↓ oxygen demand so used in ℞ of Angina & supra-ventricular arryThema (due to A.V- S.A nods)
- β_2 Blocker → Peripheral VasoconstricTn
- not effect ↓SBP ↓DBP ē no Postural hypotension

② Respiratory S

- β_2 Blocker → Bronconstrictn so CI in COPD, asthma

③ urinary S

- β Blocker → ↑ B flow To kidney → ↓ Na^+ retension → ↓ Plasma V → ↓ C.op → ↓ BP so used ē Diuretics

④ in glycogen metabolism

- β Blocker → ↓ glycogenolysis ↓ glucagon release so given ē causin ē insulin ...

B. Therapeutical uses

1. ℞ of HyperTension
2. " " migraine
3. ē HyperThyroidism ??? → ↑ sympathatic stimulatn → Cardiac arryThema.
4. ℞ of glucoma → ↓ IOR as vasocontrictn in Blood vessels feeding & ciliary body which responsible for formatn of aq-humour.

N.B not affect on ability of eye To focus for near vision unlike other Cholinergic drugs.

- used in ℞ of Acute glucoma But chronic glucoma → Pilocarpine

5. Angina - myocardial infarctn

N.B - Isoproterenol < β_1 β_2 Agonist so Blocked by Propranolol

- Epinephrine < β_1 β_2 } blocked by prop. ; α_1 → not affected
- Nor Epinephrine α only so not affected ē propranolol.

C. Adverse effect

1. Broncho ConstricTn CI in asthma. COPD → ↓ air entering & lung → Asphyxia → Death
2. ArryThemia - If quickly stopped & ℞ so & stopped must be gradually
3. Sexual impairment ♂
4. Disturbance in metabolism → insulin dependent Patient + β Blocker ↓ hypogly. & hyperglycamia

N.B Patient ē Diabetic, asthma must not be ℞ ē β Blocker + Cardio selective β_1 Blocker

D. interActn

1. propranolol + ↓ its metabolism → ↑ effect
   e.g. • Cimetidine (H_2R in stomach Block)
   • furosemide (Diruitics)
   • Chromopromazine (antipsychotic)
2. Propranolol + ↑ its metabolism → ↓ effect
   • Barbiturates
   • rifampin (anti TB)
   • phenyTain (antiepileptic)

ⓐ Actions :

i) Cardiovascular :

(*) → it ↓ COP by -ve inotropic , -ve chronotropic , -ve dromotropic effects. → this bradycardial effect limits the dose of drug to be taken

(*) → Cardiac work , oxygen demands are ↓ by B_1 block ∴ useful in angina treatment.

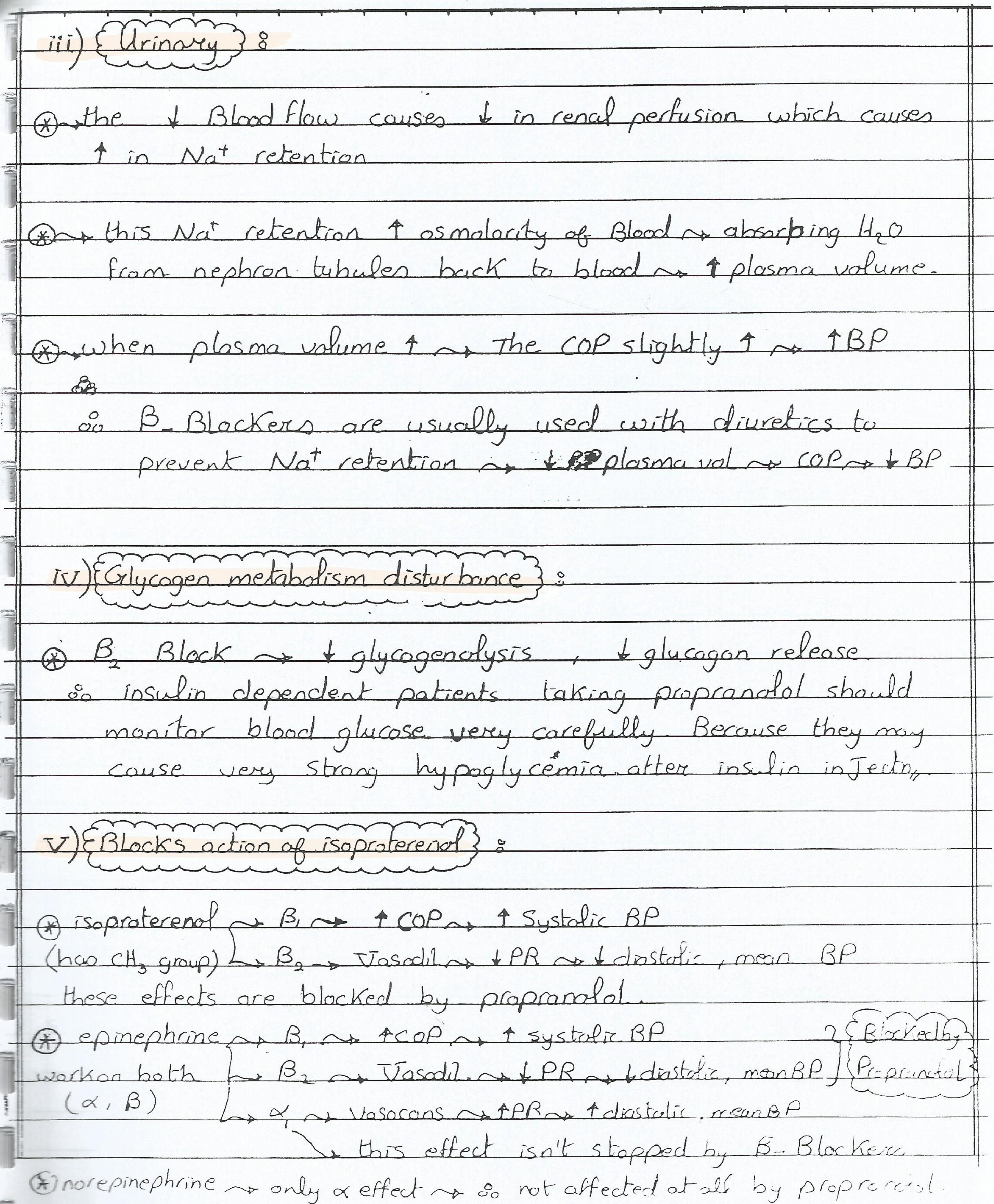
(*) → useful in case of supraventricular arrhythmias which is the arrhythmia of S.A. node , A.V. node
supraventricular ← ventricles الحاجات اللي فوق ال
(But) → not useful in case of ventricular arrhythmias

(*) Peripheral Vasoconstrictn → ⓐ By blocking B_2 which causes vasodilatatn
→ ⓑ the decrease in BP → due to ↓ COP induces reflex vasoconstrictn

(*) the net effect is gradual ↓ in systolic , diastolic BP. But with no postural hypotension (α_1 isn't affected)

ii) Respiratory :

(*) → Blocking (B_2) may cause Bronchiolar smooth Ms contractn , this can cause a respiratory crisis in patients chronic obstructive pulmonary disease or Asthma
∴ B_1 Blockers are contraindicated in patients with asthma.



iii) Urinary :

(*) → the ↓ Blood flow causes ↓ in renal perfusion which causes ↑ in Na^+ retention

(*) → this Na^+ retention ↑ osmolarity of Blood → absorbing H_2O from nephron tubules back to blood → ↑ plasma volume.

(*) → when plasma volume ↑ → The COP slightly ↑ → ↑BP

∴ B_Blockers are usually used with diuretics to prevent Na^+ retention → ↓ plasma vol → COP → ↓ BP

IV) Glycogen metabolism disturbance :

(*) B_2 Block → ↓ glycogenolysis , ↓ glucagon release
∴ insulin dependent patients taking propranolol should monitor blood glucose very carefully Because they may cause very strong hypoglycemia after insulin injection.

V) Blocks action of isoproterenol :

(*) isoproterenol → B_1 → ↑ COP → ↑ Systolic BP
(has CH_3 group) → B_2 → Vasodil → ↓ PR → ↓ diastolic , mean BP
these effects are blocked by propranolol.

(*) epinephrine → B_1 → ↑COP → ↑ systolic BP
work on both → B_2 → Vasodil. → ↓ PR → ↓ diastolic, mean BP } Blocked by Propranolol
(α, B) → $α_1$ → Vasocons → ↑PR → ↑ diastolic , mean BP
→ this effect isn't stopped by B- Blockers

(*) norepinephrine → only α effect → ∴ not affected at all by propranolol.

(b) Therapeutic uses :

i) {hypertension} :

→ it Lowers BP by ↓ COP

ii) {Glucoma} :

→ it ↓ intraocular pressure by B_2 Block causing vasoconstriction of Blood vessels feeding ciliary body which is responsible for aqueous humour formation.

→ it has the advantage that it doesn't affect the ability of eye to focus for near vision , doesn't change pupil size as cholinergic drugs.

→ it's used only in chronic glucoma treatment But in acute attacks of glucoma → pilocarpine is the drug of choice.

iii) {Migraine} :

→ it Blocks (B_2) vasodilatation in Brain vasculature.

iv) {hyperthyroidism} :

→ hyperthyroidism causes ↑ sympathetic stimulation that may cause serious cardiac arrhythmias

الواد لو عنده hyperthyroidism بيبقى دايماً عصبي

→ this effect is ↓ by propranolol.

v) angina pectoris :

→ it ↓ HR, COP → ∴ ↓ Cardiac work

∴ ↓ oxygen requirement of heart muscle

∴ reduces chest pain on exertion (work)

∴ Propranolol is useful in chronic management of stable angina (not for acute angina attacks).

vi) Myocardial infarctn :

→ Propranolol has protective effect on myocardium.

→ it's used prophylactically to prevent a second attack in case of patient that already sufferred from one attack.

→ Propranolol administratn immediately after a myocardial infarctn may reduce size, hastens recovery.

→ it reduces the incidence of Sudden arrhythmic death after myocardial infarctn

Ⓒ Adverse effects :

- → Bronchoconstriction
- → Arrhythmia
- → Sexual Impairment
- → Disturbances in metabolism

[1] Bronchoconstriction :

احنا عارفين انه بيعمل bronchoconstriction بسبب انه بيقفل الـ β_2
طب لو المريض ده عنده asthma . يعني الـ lungs عنده
اصلاً مقفولة ← يبقى لما اديله الدواء ده ← مش هيعرف
يتنفس وهيموت

* Propranolol has a serious and potentially lethal side effect when administered to an asthmatic. why?!
- because an immediate contraction of the bronchial smooth muscles prevents air from entering the lungs

∴ Deaths by asphyxiation (عدم القدرة على التنفس) have been reported for asthmatics who were administered the drug.

∴ Propranolol must never be used in treating any individual with obstructive pulmonary disease.
وعرفنا ليه ...

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[2] Arrhythmia :

Treatment with the β. blockers must never be stopped quickly why?!
- because of the risk of precipitating cardiac arrhythmia which may be severe. As long term treatment with an antagonist leads to up regulation of the β. receptors.

يعني أي واحد بياخد الـ propranolol ما ينفعش يوقف العلاج مرة واحدة علشان هيحصله arrhythmia ، طب ليه ؟!

علشان ال antagonist ده كان قافل ال receptors ، فلما آجي أوقفها مرة واحدة ← يبقى كل ال β_2 receptors (اللى على القلب) اللى كانوا مقفولين دول هيفتحوا مرة واحدة و يشتغلوا جامد ← يعملوا arrhythmia .

∴ The β-blockers must be stopped gradually for 1 week.

- On Suspension of therapy → the increased receptors can worsen angina or hypertension → لما اوقف العلاج مرة واحدة .

---

3 **Sexual Impairment :**

دى غريبة شوية ← علشان ال male sex organs بيشتغل عليها α receptors ← فالمفروض ان ال β blockers ما تديش تأثير عليها ← لكن وجدنا برده انه بيحصل impaired sexual activity فى بعض المرضى اللى خدوا الدواء ده ← بس السبب مش معروف

* Since sexual function in the male occurs through α-adrenergic activation → β-blockers maynot affect normal ejaculation nor the internal bladder sphincter function.

---

4 Disturbances in metabolism:

نفسو بيقفل الـ β_2 receptors اللى بتزود الـ glycogenolysis
والـ glucagon secretion ← ↑ glucose ← hyperglycemia
يبقى لما اقفل الـ receptors دى ← ↓ glycogenolysis و
↓ glucagon secretion ← ↓ glucose ← hypoglycemia
. حلو كده !! طب فين المشكلة بقى !!

المشكلة لو حده مريض عنده diabetes بس من النوع الـ insulin dependant
دول بياخد insulin علشان يقلل الـ glucose اللى ف الدم و الدواء
اصلاً عامله hypoglycemia ← يبقى الـ glucose عنده هيقل
بطريقة حادة أوى وخطر .

* β - blockers leads to ↓ glycogenolysis and ↓ glucagon secretion → ∴ Fasting hypoglycemia may occur.

يبقى لو عايز اقلل الضغط لواحد عنده asthma او insulin dep diabetes
يبقى مش هينفع استخدم الـ non selective β - blockers لكن استخدم حاجة
selective بتشتغل بس على الـ β_1 ←

∴ Cardioselective β - blockers are preferred in treating insulin dependant asthmatics.

دلوقتى هنشوف آخر حدوته فى الـ Propranolol وهى الـ
Drug Interactions.

(d) Drug Interactions :

طبعي ان اى ادوية تقلل تكسير او ال metabolism بتاع ال propranolol ← هتزود ال effect بتاعه

وأى ادوية بتزود ال metabolism بتاعه ← بتكسر اكتر ← هتقلل ال effect.

* Drugs that interfere with the metabolism of propranolol as :
  - Cimetidine (H2 blocker for peptic ulcer)
  - furosemide (diuretic)
  - chlorpromazine (antipsychotic)

  → potentiate its antihypertensive effect.

- while, drugs that stimulate its metabolism, such as :
  - barbiturates
  - phenytoin (antiepileptic)
  - rifampin (anti TB)

  → ↓ its effect.

---

(2) Timolol and Nadolol

*معلومة ليك لتسهيل الحفظ ←

كل ال β- blockers آخر اسمهم (-olol)

ماعدا ال Labetalol وال carvedilol ← آخرهم (-lol) بس.

حبيت نقولوا نقول كلمتين كده على الدوايين دول ← مش هنطول زي ال Propranolol oooo

2) Timolol - Nadolol β Blocker

- Non selective β Blocker < β_1, β_2
- More Potent Than Propranolol
- Nadolol → v. long duratn of Actn
- Timolol → ↓ productn of aqueous humour in eye
  So used in of open angle glucoma
  and hypertension

* Timolol & Nadolol are non selective β- blockers (i.e. block β_1 & β_2 adrenoceptors)

بحيث زي ال Propranolol ، بس الفــــرق ↙

they are more potent than Propranolol.

* Nadolol → has a very long duration of action

* Timolol → ↓ the production of aqueous humor in the eye & is used topically in the ttt of chronic open - angle glaucoma

  - also used occasionally for systemic treatment of hypertension.

بس كده ← خلصنا الاتنيــن دول ← شايفنين السرعة ٥ ٥ ٥

---

③ Acebutolol, Atenolol, metoprolol and Esmolol

↓

Selective β_1 antagonists.

دول selective بحيث بيشتغلوا على نوع واحد من ال receptors اللي هــو β_1 (بتاع القلب) ← يبقى ممكن استخدمهم علشان اقلل الضغط واتفادى ال unwanted bronchoconstrictor effect اللي كان بيديه ال propranolol في ال asthmatic patients بسبب تأثيره على ال β_2 receptors.

β_1 selective B [3] 1) Atenolol - 2) Esmolol - 3) metoprolol - 4) Acebutolol - 5) pindolol

• β_1 selective B. They are Antagonist for β_1 but does 50-100 times less than Those required for β_2 R.

* Acebutolol, pindolol have intrinsic Agonist Activity (Partial Agonist)

A Actn

- ↓ COP - ↓ HR
→ ↓ B.P so used in Tx of Angina & Hypertension
• Esmolol have short lifetime as metabolise c̄ ester linkage
→ I-V
→ β_2 X so no Bronchoconstrictn

B uses

- Cardioselective B Blocker is useful for hypertensive patient c̄ COPD or insulin dependent patient asib avoid β_2 effect

A Actn

- Antagonist with Partial Agonist Activity
- have intrinsic sympathetic activity (ISA)
i.e have lability of weakly stimulated β_1, β_2 Rs
- ↓ lipid, Carbohydrate metabolism.

B Therapeutical uses

(1) Tx of hypertension c̄ moderate Tachycardia why???

(2) Tx of diabetic

* طب هو ازاى selective β_1 يعنى اشمعنه هيمسك فى ال β_1 بس ؟!

ده بسبب اننا بنحتاج منه dose قليلة علشان يدى تأثير على ال β_1 receptors .. يعنى ايه برده ؟!
يعنى مثلاً لو اديت dose عبارة عن 50mg ← دى كافية انها تدى تأثير وتمسك فى ال β_1 receptors بس مش هتمسك فى ال β_2 receptors ← يعنى selective
لكن لو زودت ال dose ← مثلاً 150mg ← كده هيمسك فى الاتنين β_1 & β_2 وكده مبقاش selective خلاص ...
نكتب الكلام ده بقى ....

* Cardioselective β_1 blockers, such as: Acebutolol, Atenolol, and Metoprolol → antagonize β_1 receptors at doses 50 → 100 times less than those required to block β_2 receptors.

∴ This Cardioselectivity is thus most pronounced at low doses and is lost at high drug doses.

N.B: Acebutolol has some intrinsic agonist activity

• يعنى ايه ؟!

- الطبيعى فى ال antagonists انهم بيمسكوا فى ال receptor ويقفلوه فيمنعوا ال agonist من انه يمسك فيه ← يعنى يعملوا blocking ← ده اللى احنا عارفينه ← حلو كده؟!

امال ايه ماله ال Acebutolol ده ؟!
- ده بقى بيمسك برده فى ال receptor ويمنع ال agonist من انه يمسك فيه ← بس مش بيعمل complete blocking

لكن بيدي effect بسيط زي الـ agonist ← بنسميه Partial agonist.

فهمتوا بقى الفرق بين الـ agonist, antagonist, partial agonist ؟!

agonist ← يمسك في الـ receptor ويدي effect

antagonist, partial ← يمسكوا في الـ receptor ويمنعوا الـ agonist انه يمسك بس

antagonist ← مش هيدي effect

Partial agonist ← هيدي effect بس اقل من الـ agonist

يارب تكون وصلت حلو ....

طب هنشوف ايه حاجتين دلوقتي ؟

1. actions
2. Therapeutic uses.

(1) Actions :

احنا هنتكلم عن الـ atenolol, metoprolol, esmolol ← اما الـ Acebutolol فنسيبه ← هنتكلم عليه بعد شوية ...
يعني احنا اللي بنتكلم عنهم دلوقتي هم antagonists عاديين ...

* These drugs ↓ blood pressure in hypertension & ↑ exercise tolerance in angina

* Esmolol has a very short lifetime due to metabolism of an ester linkage

بيتكسر بسرعة ← فيطلع من الجسم بسرعة

∴ It's only given IV if required during surgery or diagnostic procedures.

* In contrast to Propranolol (Non selective) ⟶ these Cardiospecific blockers have relatively little effects on pulmonary function, peripheral resistance (no α effect), and Carbohydrate metabolism (no effect on β_2 receptors)

However, asthmatics treated with these agents must be carefully monitored to make certain that respiratory activity is not compromised.

علشان احنا قلنا ان ال dose لو كترت ← مش هيبقى selective

وهيمسك ال β_2 ← اللي ممكن تعمل bronchoconstriction ←

فلازم اضبط ال dose حلو أوي بالذات لو عنده asthma.

---

② Therapeutic Uses:

مادام هو selective ← يبقى استخدمه لتقليل الضغط عند مريض

عنده مشكلة من ال Pulmonary fn او عنده diabetes

وبياخد insulin (لان احنا قلنا ان ال propranolol ← انه ممكن

يعمل Fasting hypoglycemia) لكن هنا هيبقى التأثير على القلب

بس ← مالوش دعوة بحاجة تانى.

* The Cardioselective β-blockers are useful in hypertensive patients with impaired pulmonary function

also useful in diabetic hypertensive patients who are receiving insulin or oral hypoglycemic agents.

* Since these drugs have less effect on peripheral vascular receptors → ∴ Coldness of extremities (a common side effect of β- blocker therapy) is less frequent.

---

④ Pindolol and Acebutolol

↓

antagonists with Partial agonist activity

احنا خلينا خلصين القصة دي في ال acebutolol ← انا معرفش هو محطوط هناك معاهم ليه ← بس هو هنا اصح .

① Actions :

⊕ Cardiovascular :

* Acebutolol and Pindolol are not pure blockers → instead they have the ability to weakly stimulate both β_1 & β_2 receptors & are said to have intrinsic sympathatic activity (ISA)

يعني بيبه شوية sympathatic effect.

* These partial agonists stimulates the β- receptors to which they are bound → yet they inhibit stimulation by the more potent catecholamines, epinephrine & norepinephrine (agonists)

يعني هيدي effect بس ابسط بكتير من ال effect بتاع ال agonists واكتر طبعاً من ال antagonists .

∴ Produces a much diminished effect on cardiac rate & cardiac output, compared to β- blockers without ISA.

---

(2) Decreased Metabolic effects:

* Blockers with ISA → ↓ disturbances of lipid & Carbohydrate metabolism seen with other β-blockers.

---

(2) Therapeutic Uses:

* β- blockers with ISA are effective in hypertension, with moderate bradycardia → since a further ↓ in heart rate is less pronounced with these drugs

وده بسبب الـ Partial agonist effect ← يعني هيقفل الـ receptors من الـ normal agonists ← وبالتالي هيقلل الضغط لكن في نفس الوقت مش قافلة completely ← بس effect خفيف ← فمش هيعمل bradycardia جامد .

يعني لو مثلاً الـ antagonist العادي هيقلل الـ heartrate من 70 ← 20 ← مثلاً يعني .

لكن الـ partial agonist ده هيقلل من 70 ← 40

يبقى هو عمل برده bradycardia بس اقل من الـ complete blockers ماشي !!

[4] labetalol (α, β Blocker)

A Action

- α Blocker → vasodilatn
→ ↓ PR → ↓ BP
- β Blocker → vasoconstn
→ ↑ PR → ↓ BP

net

∴ Cause peripheral vasodilatn unlike other β Blocker, produce peripheral vasoconstrictn

→ doesn't alter serum lipid or blood glucse level

B uses

① Tt of Hypertension in patient → ↑ peripheral vascular resistant (black hypertensive patient)

② alternative of hydralazine (Tt hypertensive pregnancy)

C adverse effect

* orthostatic hypotension

* Carbohydrate metabolism is less affected with acebutolol & pindolol, than it is with Propranolol
∴ they are valuable in the treatment of diabetes.

---

⑤ Labetalol

↓

يعني في نفس الوقت

Reversible β- blocker with concurrent α- blocking actions

يعني بيقفل الـ α, β ← طب لما يقفل الـ α ← هيحصل ايه ؟!
هيعمل vasodilatation وهيقلل الـ blood pressure عن طريق
انه هيقلل الـ peripheral resistance
لكن اللى كانوا بيقفلوا الـ β بس ← كانوا برده بيقللوا الـ B.P.
بس كانوا بيعملوا vasoconstrictn وبيزودوا الـ peripheral resistance

---

* Labetalol cause peripheral vasodilation → ∴ ↓ blood pressure
∴ Contrasts with other β- blockers that produce peripheral vasoconstriction
∴ It's useful in treating hypertensive patients for whom increased peripheral vascular resistance is undesirable

* Labetalol doesn't alter serum lipid or blood glucose levels.

(1) Therapeutic Use in hypertension:

* Labetalol is useful for treating the elderly or black hypertensive patients

يعني مراحل متأخرة او severe من ال hypertension ← المهم فيها ان

increased peripheral vascular resistance is undesirable

[In general, black hypertensive patients are not well controlled by β- blockers]

فاستخدملهم الـ α- blockers زي ال labetalol.

* Labetalol may be employed as an alternative to hydralazine in the treatment of pregnancy induced hypertension.

يعني عايزه يقلل لي الضغط من غير ما يعمل vasoconstrictⁿ

(2) Adverse effects:

دوخة

Orthostatic hypotension & dizziness are associated with α- blockade

يعني ايه Orthostatic hypotension ؟!

ده اللي هو لما يجي يقف مرة واحدة يدوخ ... ليه ؟!

علشان ال α-blockers دول عاملين hypotension ← وفي نفس

الوقت عاملين peripheral vasodilation ← فالانسان ده لما يكون قاعد

او نايم ← الدم كله هينزل لتحت وماقيش resistance لنزول الدم

ده ← فلما يجي يقوم مرة واحدة ← مفروض الطبيعي ان ال α-receptors

[5] Bisoprolol β1 Blocker

- selective β1 B ē ISA
- Bisoprolol → + ACEC (~~Acetyl choline - esterase~~) inhibitor
  → + Diuretics

- Ⓣ of chronic heart failure
- Ⓣ of hypertension.

→ - Cause bradycardia - hypotension - fatigue

→ orally bioavailablity 90%

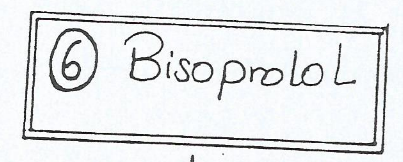
→ eliminated by renal excretn (58%)

→ metabolized in liver

→ plasma half life 11 → 17 hrs

سؤال Nadolol ≠ Bisoprolol in half life

تزود الـ B.P فيروح للـ peripheral vessels اللي حاجل في vasoconstriction
فيمنعه انه ينزل ← كده التضبيط والـ brain وصله دم كويس .
لكن لما اقفل الـ α receptors ← الـ brain مش واصله دم لفاية
← يدوخ ويحس انه هيغمى عليه ← اسمه Orthostatic hypotension



⑥ Bisoprolol

↓

highly selective β_1 receptor antagonist that has no ISA or membrane stabilizing activity.

* Bisoprolol is well tolerated and side effects include : dizziness, bradycardia, hypotension & fatigue.

* Bisoprolol can be considered a standard treatment option when selecting a β- blocker for use in combination with ACE (Acetylcholine esterase) inhibitors & diuretics in patients with moderate to severe chronic heart failure & in treating hypertension.

* Bisoprolol is well absorbed after oral administration with bioavailability of ≃ 90%
- It is eliminated by renal excretion (50%) & liver metabolism to pharmacologically inactive metabolites (50%)
- It has plasma half life of 11 → 17 hrs.

يعني long duration of action ← بس اطول واحد هو ؟! فاكرين !؟
Nadolol →
bravo عليا

[6] Carvidilol β_1, β_2, α_1 Receptor

- like labetalol ويزيد عليه → Antioxidant & anti proliferating effect
  → membrane stabilizing Activity ???
  Depolarization عكس

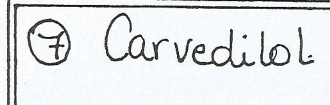
- Lack ISA

- α_1 Blocker → vasodilatn & antioxidant & anti proliferating so used in III at Congestn Heart failure (CHF) ???

- is rapidly absorped in oral → Plasma Conc. 1→2hrs and as it lipophilic distributed in → interstitial fluid (half life 7-10hr)

- first Pass effect

وآخر دواء معانا في ال 8 β- Blockers



↓

third generation β receptor antagonist that has a unique pharmacological profile.

↓

It blocks β_1, β_2 & α_1 receptors (similar to Labetalol)

بس زيادة عليه كمان عنده ←

a- antioxidant & antiproliferative effects.

b- membrane stabilizing activity →

زي ال anaethetics ← بيعمل stabilization لل Na^+ ← فتمنع

هيحصل depolarization ← فال cell هتشتغل ← عمل anaethesia

c- It lacks intrinsic sympathomimetic activity.

* Uses & Action:

- Carvedilol produces vasodilation (due to α_1 blocking).
- It is thought That the additional properties (antioxidant and antiproliferative effects) ⟶ contribute to the beneficial effects seen in treating Congestive heart Failure. (CHF)

يعني بيستخدم ال Carvedilol ده علشان يعالجوا ال CHF

طب اشمعنى ؟!

علشان في ال CHF ← بيحصل Cardiomegaly يعني حجم القلب بيكبر

يعني حصل proliferation ← وال Carvedilol عنده antiproliferative effect.

* Carvedilol is rapidly absorbed following oral administration (peak plasma conc. occur in 1 → 2 hrs)

* It is highly lipophilic → ∴ rapidly distributed in extravascular tissues (interstitial fluid)

* It is 95% protein bound & extensively metabolized in liver.

* It's half life from 7 → 10 hrs.

يعني هو بيحصله absoption بسرعة ← بيزيد في الـ plasma خلال
ساعة او ساعتين ← وبيروح من الـ plasma للـ interstitial fluids
لانه highly lipophilic ← لكن في كمية كبيرة منه 95% بتمسك
في الـ protein وبالتالي مش هتدخل الخلية وهتتكسر في الـ liver
واللي بيدخل الخلية 5% بس.

غير انه ممكن يحصل له كمان 1st pass effect لانه اتاخد oral
بس ده مش بيحصل لكله ...

Stereoselective 1st pass metabolism results in more rapid clearance of S(−) Carvedilol than R(+) Carvedilol
↓
هيتكسر اكتر

كده خلصنا الـ α Blockers ووراها الـ β- Blockers وشفنا
الادوية اللي عليهم ... دلوقتي هنشوف نوع جديد ← هو برده antagonist
بس بطريقة مختلفة ← يلا اقلب علشان نشوفه

Drugs affecting Neurotransmitter Release or uptake

افتكر معايا كده فى ال agonists ← كنا قلنا انه مش كله لازم يشتغل على الـ receptor نفسه ← لكن فى ادوية زى الـ amphetamine & tyramine دول بيزودوا الـ effect بردو بس عن طريق انهم يزودوا الـ release بتاع الـ Neurotransmitter من الـ storage vesicles. ← صح ؟!

طيب ، هنا نفس الفكرة ← انا هغير الـ effect بس من غير ما اجى جنب الـ receptor ← انا هشتغل على الـ neuron ← يا إما اقلل الـ release بتاع الـ neurotransmitter ← يا إما اقلل الـ uptake بتاع الـ neurotrans. فى الـ storage vesicles ← ↓ effect.
او هقلل الـ reuptake فى الـ nerve ← ↑ effect زى الـ cocaine

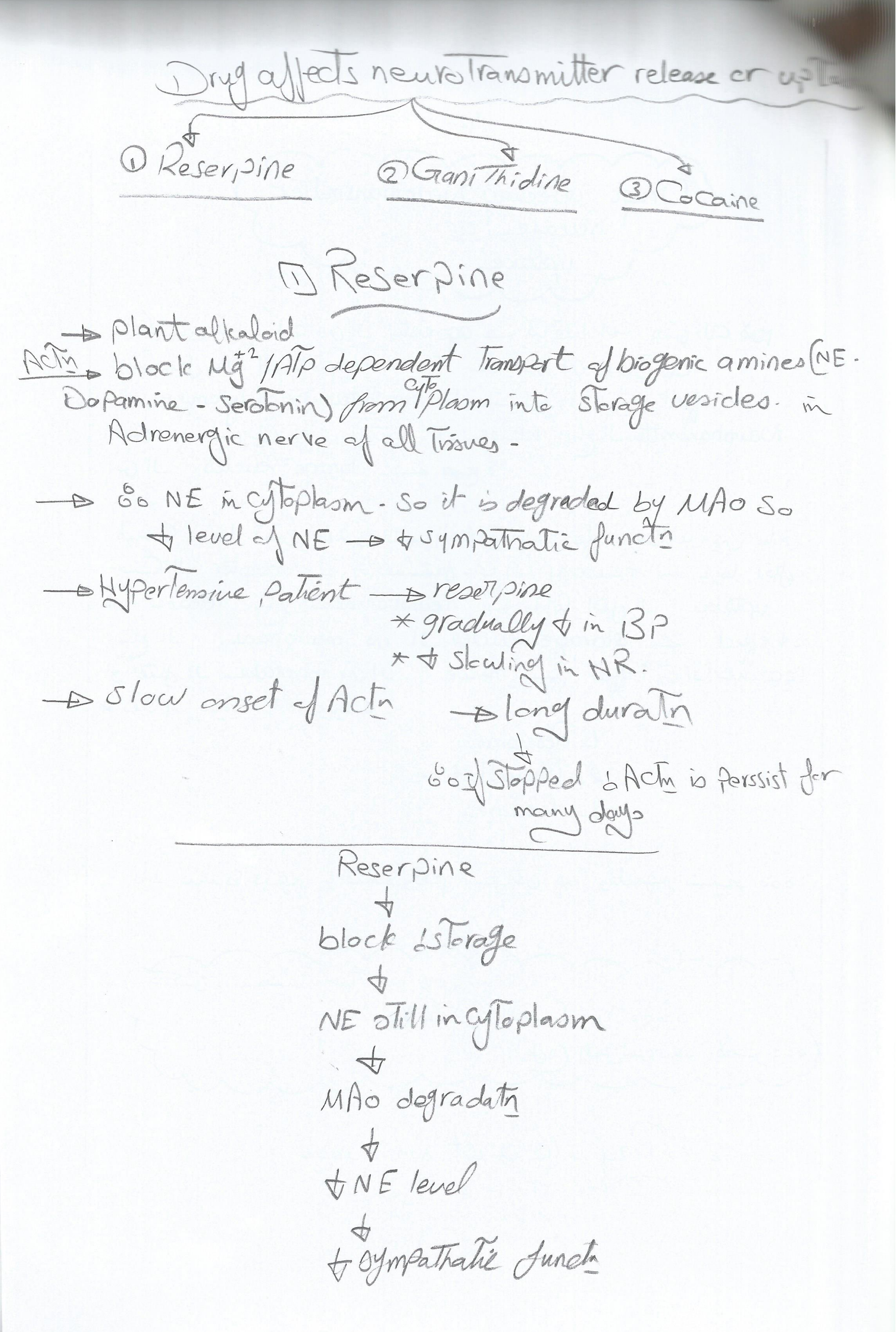
* هناخد فيه ٣ ادوية :

1- Reserpine
2- Guanethidine
3- Cocaine

يلا نبتدى فيهم وهتلاقوهم سهلين جداً وكلامهم بسيط ...

كن مطمئناً جداً جداً ....
ولا تفكر فى الامر كثيراً ....
بل دع الامر لمن بيده الأمر ...

...... Pray 4 us a lot ......



Drug affects neuroTransmitter release or upTa

① Reserpine ② GaniThidine ③ Cocaine

[1] Reserpine

→ plant alkaloid

Actn → block Mg^{+2}/ATP dependent Transport of biogenic amines (NE - Dopamine - Serotonin) from cytoplasm into storage vesicles in Adrenergic nerve of all Tissues -

→ ∴ NE in cytoplasm - so it is degraded by MAO so ↓ level of NE → ↓ sympathatic functn

→ Hypertensive patient → reserpine
- * gradually ↓ in BP
- * ↓ slowing in HR.

→ slow onset of Actn → long duratn → ∴ If stopped ≀ Actn is perssist for many days

---

Reserpine
↓
block ≀ storage
↓
NE still in cytoplasm
↓
MAo degradatn
↓
↓ NE level
↓
↓ sympathatic functn



1 Reserpine

* Reserpine, a plant alkaloid → blocks the Mg^{+2}/ATP dependant transport of biogenic amines (norepinephrine, dopamine & serotonin) from the cytoplasm into the storage vesicles in the adrenergic nerves of all body tissues.

يعني احنا عارفين ان ال norepinephrine بيتحمل في ال nerve
ويتخزن في ال storage vesicles لحد وقت ما يحصل excitation وبعدها
release ← تمام؟!
طب ال reserpine ده هيوقف تخزين ال norepinephrine
← فهيفضل في ال cytoplasm ← طب ايه المشكلة؟! المشكلة ان
ال cytoplasm فيه MAO ← اللي بيكسر اي free norepinephrine
في ال cytoplasm

Monoamineoxidase (MAO) can degrade the norepinephrine in the cytoplasm → this causes an ultimate depletion (i.e decrease) of norepinephrine levels in the adrenergic neuron.

∴ Sympathatic function, in general, is impaired due to ↓ release of Norepinephrine.

* Hypertensive patients taking the drug shows a gradual ↓ in blood pressure & slowing of the cardiac rate
- The drug has a slow onset of action but long duration of action

* slow onset ← علشان عقبال ما يوقف ال storage وال MAO

2 GuaniThidine

Actn → Inhibits the response of Adrenergic nerve to stimulatn or any indirect Acting sympathomimetics amin.

How???

1. block the release of E. from the storage vesicals → ↓NE → ↓BP → ↓HR → ↑Parasympathomimitic in GIT
2. Displace the NE in storage vessicales → ↑BP

S.E → orThostatic Hypotension. interfere c̄ male sexual functn

~ → in patient c̄ pheochromocytoma supersenistivity to NE due to ↓ release ???

↑ Cold preparatn c̄ phenyl propandamine

يبتدي يكسر الـ Free N.E. غير انه لسة هيافض وقت لحد ما يخلص
اللى كان متخزن اصلاً

والـ long duration of action ← لان هنا مش هيقفل الـ receptor شوية

واسيبه ← لا انا ↓ من الاصل ← يعني اصلاً مش هيكون فى
Norepinephrine في الـ storage vesicles علشان يطلع
وعلشان كده ←

when one stops taking the drug → the action persists for many days.

لحد ما يصنع new norepinephrine بدل اللى كسره الـ MAO

---

[2] Guanethidine

* It inhibits the response of the adrenergic nerve to stimulation or to indirectly acting sympathomimetic amines
  ↳ how?!

1- by blocking the release of stored epinephrine from the storage vesicles
→ this results in gradual ↓ of blood pressure in hypertensives & a ↓ in cardiac rate.
also there is remarkable ↑ in parasympathatic tone of the GIT ..

2 - Guanethidine also displaces norepinephrine from storage vesicles (thus producing transient ↑ in blood pressure)

يعنى بيدخل جوه الـ storage vesicles ويطلع الـ Norepinephrine
بره ← وبالتالى هيحصل زيادة فى الـ BP بس حاجة لحظية يعنى
وبعدين هيقل .
طبعاً الـ NE اللى بيطلع بره ده هيتكسر ↙

∴ this leads to gradual ↓ of NE in nerve endings except those in the CNS.

* Guanethidine is now rarely used in the treatment of hypertension → as it commonly causes orthostatic hypotension & interfers with male sexual function.

النقطة اللى جاية دى الدكتور ما قلهاش ...

* Supersensitivity to NE due to depletion of amine can result in hypertensive crisis in patients with pheochromocytoma
ده tumor فى الـ adrenal medulla
يعنى هتقلل تفريغ الـ NE غير الـ Guanethidine
هيقل كمان اللى فاضل ← فالـ receptors هتبقى
supersensitive يعنى اقل كمية من الـ NE تشوفها ←
هتدى effect جامد جداً ← ممكن تعمل hypertensive crisis

* due to supersensitivity → patients taking cold preparations containing phenylpropanolamine also may have exaggerated hypertensive response.

* ودى برده ما اتقالتش ..

ده بيدى symp. effect جامد اوى

[3] Cocaine

ActIn → block Na^+/K^+ ATPase which required for reuptake of NE by Adrenergic neuron

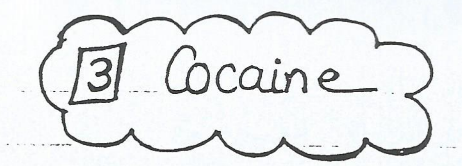
↓

NE is Accumulate in synaptic cleft

↓

↑ sympathatic Activity

So ↓ Dose of Catecholamines ē individual taken Cocaine
This magnified effect and ↑ duratn of Actn



احنا عارفين ان ال NE بعد ما بيطلع في ال synaptic cleft في حبة

منه بيدخلوهم في ال nerve reuptake ويتكسروا بال MAO

← ال Cocaine بيوقف ال uptake ده ← وبالتالي

ال NE هيفضل في ال synaptic cleft ← ↑ sympathatic activity

* Cocaine is unique among local anesthetics in having the ability to block the Na^+/K^+ Atpase (required for cellular uptake of NE) across the cell membrane of the adrenergic neuron

→ ∴ NE accumalates in the synaptic cleft → resulting in enhancement of sympathatic activity & potentiation of the actions of epinephrine & NE.

∴ Small doses of the catecholamines produce greatly magnified effects in an individual taking cocaine as compared to one who is not.

* In addition, the duration of action of epinephrine & NE is increased.

يعني اللي واخد cocaine هيكون عنده كمية ال NE اللي في ال synaptic cleft كبيرة ← يبقى لو اديته كمية قليلة من ال catecholamines ← هتدي effect جامد ← يعمل vasoconstriction ← يبقى ال anethetic هيفضل في اماكنه ده

Reserpine → prevent uptake of NE into storage vessicales.

GuaniThidine → prevent release of NE into synaptic cleft

Cocaine → prevent reuptake of NE into Neurons.

يبقى نجمعهم كده ٥٥٥٥

الدواء اللي ٥٥٥

1- prevent uptake of NE into storage vesicles
ঃ Reserpine

2- prevent release of NE into synaptic cleft.
ঃ Guanthedine

3- Prevent reuptake of NE into neuron
ঃ Cocaine

بس كده ٥٥٥

خلصنا المحاضرة وخلصنا الـ autonomic كله

* المرة الجاية د/ ابتهال ان شاء الله هتكمل معانا الـ Cardiovascular اللى ابتديناه فى المحاضرة الخامسة.
حاولوا تحضروا المحاضرة علشان الدكتورة دى شرحها حلو أوى وبتفهم حلو ٥٥٥ هتستفيدوا لو حضرتوا ٥٥٥

Plz ... Pray 4 us a lot ...
محتاجين فعلاً صلواتكم أوى ٥٥٥

Urs : Dr/P.S.
Dr/K.A.